## REMARKS

**In the Claims:**

Claims 22-26 are currently pending.

Applicants respectfully request that the Examiner consider the following remarks in response to the Office action mailed 6/13/06.

**Rejection under 35 U.S.C. § 101:**

Claims 22-26 stand rejected under 35 U.S.C. § 101 for alleged lack of utility. Applicants respectfully disagree with the rejection of these claims. As previously stated, Applicants maintain that the claimed PRO361 antibodies are supported by an adequate utility based upon the data derived from the MLR assay, as disclosed in Example 34 of the instant specification. Example 34 illustrates that the PRO361 polypeptide tested positive in the MLR assay. Therefore, the PRO361 polypeptide is an immunosuppressor, which has utility in the treatment of conditions where the suppression of an immune response would be beneficial. Antibodies to such a polypeptide would have utility in preventing suppression of the immune system, for example in cancer and HIV treatments.

Also as stated previously, in at least two related cases, U.S. Patent Application Serial No. 09/944,929, which claims the PRO361 nucleic acid and U.S. Patent Application Serial No. 10/677,471, which claims the PRO361 polypeptide, the Office has acknowledged that, in view of US Patent No. 5,817,306, "the MLR assay is art recognized for identifying molecules which suppress an immune response." *See* page 6 at Tabs A and B of the Request for Continued Examination mailed 22 March 2006. Despite this recognition by the Office in related cases, in the present application, the Office action states that "[t]he results of the assay are not predictive as Kahan clearly states that no *in vitro* immune assay predicts or correlates with *in vivo* immunosuppressive efficacy." Page 3 of the Office action mailed 6/13/06. Applicants

respectfully submit that this position is in error as the Office already has recognized that the MLR assay is art recognized for identifying immunosuppressors.

In addition to failing to recognize the MLR assay as an appropriate assay for identifying immunosuppressive molecules, it appears that the rejection of the claims is based on a misunderstanding of MLR assay as that assay was used in connection with the present invention. For example, this misunderstanding is indicated by the discussion of the MLR assay in general and "controls" for this assay, which is found on pages 4 and 6 of the Office Action mailed 6/13/06. Applicants respectfully submit that the controls discussed in the Office action are only needed when the purpose of the MLR assay is to evaluate the properties of the stimulator cells. In contrast, the purpose of the MLR assay disclosed in the instant specification and used in the present invention is to characterize, not the stimulator cells, but the test proteins such as PRO361. Specifically, the mixing of the stimulator and responder cells in the MLR assay as described in the instant specification is expected to lead to T cell proliferation. The point of the assay is not to measure the T cell proliferation but rather the extent to which the test protein can suppress the expected proliferation of the stimulated T cells. Indeed, the precise extent to which the stimulator cells stimulate the responder cells is not significant; what matters is whether the test protein decreases this response.

The extent to which the test protein decreases the response of the T cells is measured by comparison to a negative control reaction, which uses either cell culture medium, or a non immunostimulant molecule, CD4-IgG, as a negative control. Because the response in the test reaction is compared to a negative control reaction, and because both reactions use the same stimulator and responder cells at the same time, additional controls to determine the precise properties of these cells are not required. In addition, explicit data values on the exact percentage of decrease below control are not necessary, particularly because the specification specifically teaches that decreases below control are significant because they indicate a positive result. The specification further characterizes decreases of 80% below control as being preferred but such decreases are not described as necessary.

Further, explicit data values are of the decrease observed in the MLR assay described in the specification are not necessary to satisfy the utility requirement for claims 22-26. The MLR assay described in the present specification is a comparative assay, meaning that the utility of PRO361 demonstrated by this assay is based upon a comparison of relative expression levels between a known molecule and the unknown PRO361 molecule. Useful information is obtained when relative differences are observed, and this is routine in biological testing. All that is important for utility is that the difference is significant. And Applicants expressly assert that the difference for PRO361 immunosuppression as observed in the MLR assay described in the specification is significant. For example, the specification expressly states that, in the instant MLR assay, decreases below control are significant because they indicate a positive result, decreases of greater than or equal to 80% are preferred, and PRO361 tested positive in this assay. The Office action seems to focus on exactly what was the decreased value below control (*i.e.,* requiring Applicants to provide "relative or absolute levels" and statistical analyses), but Applicants submit that this exact value is not relevant to the issue at hand, nor is it required for the claimed invention to be useful.

Further, based on the identification of the PRO361 polypeptide as an immuno-suppressive molecule, one skilled in the art would find it credible that antibodies to PRO361 are useful where suppression of the immune system is not desired, for example in cancer and HIV treatments. Yet, based on the lack of explicit data in the specification, the Office action asserts that "further experimentation would be required to use the invention in this manner."

Applicants respectfully disagree. Regarding the need for "values or data for the proteins tested in the assay" or "statistics for the values measured," these remarks are a clear indication that the Office action applies a standard that might be appropriate if the issue at hand were the regulatory approval of a drug based on the immunosuppressor activity of PRO361, but is fully inappropriate for determining if the "utility" standard of the Patent Statute is met. The FDA, reviewing an application for a new immunosuppressor drug, will indeed ask for actual numerical data, statistical analysis, and other specific information before the drug is approved. However, the Patent and Trademark Office is

not the FDA, and the standards of patentability are not the same as the standards of market approval. It is well established law that therapeutic utility sufficient under the patent laws is not to be confused with the requirements of the FDA with regard to safety and efficacy of drugs marketed in the United States. *Scott v. Finney*, 34 F.3d 1058, 1063, 32 U.S.P.Q.2d 1115, 1120 (Fed. Cir. 1994). Indeed, in *Nelson v. Bowler,* 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (C.C.P.A. 1980), the Federal Circuit found that the identification of a pharmacological activity of a compound provides an "immediate benefit to the public" and satisfies the utility requirement. This logically applies to the instant utility as well. The identification of a PRO361 compound as an immunosuppressor should suffice to establish an "immediate benefit to the public" and thus to establish patentable utility.

Indeed, when understood in this context Applicants' assertion of utility is supported by and entirely consistent with the case law. For example, in *CFMT Inc .v . Yieldup Internat'l Corp.,* 68 USPQ2d 1940 (Fed. Cir. 2003), the Federal Circuit considered whether claims to an apparatus for cleaning silicon wafers satisfied the utility requirement even though neither the claims nor the specification explicitly defined "clean," *e.g.* described a specific level of removal of contaminants. According to the Federal Circuit, "[b]ecause the preamble term 'cleaning' means only 'removal of contaminants,' not removal of all contaminants or removal of contaminants according to the TI commercial standard, the inventor shows utility and enables the invention by disclosing 'removal of contaminants.'" *Id.* at 1945. So too here. Applicants have demonstrated utility of the present invention by demonstrating suppression of the immune response; that demonstration does not have to achieve any level beyond a "significant" level of suppression. The specification clearly teaches that the observed positive results observed for PRO361 are significant regardless of whether such results reach the "preferred" level of decreases below 80%. In *CMFT* the court only required that there be some meaningful result satisfying the claimed goal. Applicants respectfully submit that the specification provides evidence that a meaningful result, *i.e.* meaningful suppression of the immune response in the MLR assay, is achieved with the PRO361 polypeptide. Thus, the decrease in proliferation of cells in the MLR caused by PRO361 as compared to a negative control, which is asserted in the specification as

evidence that the PRO361 polypeptide is useful as an immunosuppressive agent, is sufficient to satisfy the utility requirement of 35 U.S.C. § 101 under the case law.

Applicants further respectfully remind the Examiner that an Applicants' assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101, "**unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope**." (emphasis added) *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974). *See also In re Jolles*, 628 F.2d 1322, 206 U.S.P.Q. 885 (C.C.P.A. 1980); *In re Irons*, 340 F.2d 974, 144 U.S.P.Q. 351 (1965); *In re Sichert*, 566 F.2d 1154, 1159, 196 U.S.P.Q. 209, 212-13 (C.C.P.A. 1977). Compliance with 35 U.S.C. §101 is a question of fact. *Raytheon v. Roper*, 724 F.2d 951, 956, 220 U.S.P.Q. 592, 596 (Fed. Cir. 1983) cert. denied, 469 US 835 (1984). The evidentiary standard to be used throughout *ex parte* examination in setting forth a rejection is a preponderance of the evidence, or "more likely than not" standard. *In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992). This is stated explicitly in the M.P.E.P.:

> [T]he applicant does not have to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt." **Nor must the applicant provide evidence such that it establishes an asserted utility as a matter of statistical certainty**. Instead, evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. *M.P.E.P.* at § 2107.02, part VII (2004) (underline emphasis in original, bold emphasis added, internal citations omitted).

The Examiner has the initial burden to offer evidence "that one of ordinary skill in the art would reasonably doubt the asserted utility." (emphasis added) *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). Only then does the burden shift to Applicants to provide rebuttal evidence. *Id.* The Examiner has not cited a single reference that would show that one of ordinary skill in the art would reasonably doubt the asserted utility. Accordingly, a proper prima facie case has not been made in this instance and the burden to rebut this rejection has not entirely shifted to the Applicants.

Yet, Applicants provided the Fong Declaration to explain how the MLR reaction was performed in the instant application using peripheral blood mononuclear cells (PBMCs).

In fact, the Fong Declaration detailed the state of the art, at the time of filing, in the field of immunostimulation/suppression and provided art accepted examples of the usefulness for such immunostimulatory and immunosuppressor molecules. Based on these teachings, it is more likely than not that one skilled in the art, to a reasonable probability, would believe that the claimed antibody is useful because it binds to an immunosuppressor. Further, the specification also provides detailed guidance on how to identify and make antibodies to PRO361 polypeptides. Thus, Applicants believe that this rejection of claims 22-26 is overcome and should be withdrawn.

**Rejection under 35 U.S.C. § 112, first paragraph:**

**Enablement**

Claims 22-26 also stand rejected under 35 U.S.C. § 112, first paragraph because allegedly one of ordinary skill in the art would not know how to make and use the claimed invention because allegedly the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicants respectfully disagree. As discussed above, the claimed antibody has the specific, substantial, and credible utility of binding a polypeptide that inhibits the proliferation of stimulated T-lymphocytes as demonstrated in the MLR assay experiment discussed in Example 34 at page 141 of the application. Applicants respectfully request the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 112 ¶1 for alleged inadequate disclosure on how to use the claimed invention.

## CONCLUSION

Applicants believe this Request for Reconsideration fully responds to the Office action mailed May 19, 2006. Applicants respectfully request the Examiner grant allowance of pending claims 22-26. The Examiner is invited to contact the undersigned attorney for the Applicant via telephone if such communication would expedite allowance of this application.

Respectfully submitted,

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